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AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (Currently Amended) A method for obtaining a pluripotent human blastocyst-derived stem cell line, ~~the method comprising: the steps of~~
 - i) using a fertilized oocyte of ~~having a~~ grade 1 or 2[[,]] to obtain a blastocyst, ~~having a~~ of grade A or B; [[,]]
 - ii) co-culturing the blastocyst with feeder cells to establish ~~for establishing~~ one or more colonies of inner cell mass cells; [[,]]
 - iii) isolating the inner cell mass cells by mechanical dissection; and [[,]]
 - iv) co-culturing ~~of~~ the inner cell mass cells with feeder cells to obtain a blastocyst-derived stem cell line.
 - ~~v) optionally, propagation of the blastocyst-derived stem cell line.~~

2. (Currently Amended) A method for obtaining a pluripotent human blastocyst-derived stem cell line, ~~the method comprising: the steps of~~
 - i) using a fertilized oocyte of ~~having a~~ grade 1 or 2[[,]] to obtain a blastocyst; [[,]] ~~optionally having a grade A or B;~~
 - ii) co-culturing the blastocyst with feeder cells to establish ~~for establishing~~ one or more colonies of inner cell mass cells; [[,]]
 - iii) isolating the inner cell mass cells by mechanical dissection; and [[,]]
 - iv) co-culturing ~~of~~ the inner cell mass cells with feeder cells to obtain a blastocyst-derived stem cell line.
 - ~~v) optionally, propagation of the blastocyst-derived stem cell line.~~

3. (Currently Amended) A method for obtaining a pluripotent human blastocyst-derived stem cell line, ~~the method comprising: the steps of~~

- i) using a fertilized oocyte ~~optionally, having a grade 1 or 2,~~ to obtain a blastocyst ~~of , having a grade A or B;~~ [[.]]
- ii) co-culturing the blastocyst with feeder cells to establish ~~for establishing~~ one or more colonies of inner cell mass cells; [[.]]
- iii) isolating the inner cell mass cells by mechanical dissection; and [[.]]
- iv) co-culturing ~~of~~ the inner cell mass cells with feeder cells to obtain a blastocyst-derived stem cell line.
- ~~v) optionally, propagation of the blastocyst-derived stem cell line.~~

4. (Currently Amended) A method for obtaining a pluripotent human blastocyst-derived stem cell line, ~~the method comprising: the steps of~~

- i) using a fertilized oocyte optionally of , ~~having a grade 1 or 2~~ [[.]] to obtain a blastocyst of [[.]] optionally ~~having a grade A or B;~~ [[.]]
- ii) co-culturing the blastocyst with feeder cells to establish ~~for establishing~~ one or more colonies of inner cell mass cells,
- iii) isolating the inner cell mass cells by mechanical dissection,
- iv) co-culturing ~~of~~ the inner cell mass cells with feeder cells to obtain a blastocyst-derived stem cell line; and [[.]]
- v) propagation of the blastocyst-derived stem cell line culturing the stem cells with feeder cells of a density of less than about 60,000 cells per cm², ~~such as e.g. less than about 55,000 cells per cm², or less than about 50,000 cells per cm², such as about 45,000 cells per cm².~~

5. (Currently Amended) The A method ~~according to any of the claim 1,~~ wherein ~~claims 1-4 in which~~ the blastocyst in step i) is a spontaneously hatched blastocyst.

6. (Currently Amended) The A method ~~according to any of the claim 1,~~ wherein ~~claims 1-5 in which~~ the blastocyst-derived stem cell line is stable.

7. (Currently Amended) The A method according to any of the claim 1, claims 1-6 wherein the blastocyst-derived stem cell line is propagated.

8. (Currently Amended) The A method of according to claim 7, wherein propagating the in which the propagation of blastocyst-derived stem cell line comprises passaging ~~passage~~ of the stem cell line every 4-5 days.

9. (Currently Amended) The A method of claim 7 according to claims 7-8, wherein propagating the in which the propagation of blastocyst-derived stem cell line comprises culturing the stem cells with feeder cells of a density of less than about 60,000 cells per cm^2 , ~~such as e.g. less than about 55,000 cells per cm^2 , or less than about 50,000 cells per cm^2 .~~

10. (Currently Amended) The A method of according to claim 9, wherein propagating the in which the propagation of blastocyst-derived stem cell line comprises culturing the stem cells with feeder cells of a density of about 45,000 cells per cm^2 .

11. (Currently Amended) The A method of claim 7, wherein according to claims 7-10, in which the propagation of blastocyst-derived stem cell line comprises passage of the feeder cells at the most 3 times, ~~such as e.g. at the most 2 times.~~

12. (Currently Amended) The A method of claim 1, wherein according to any of the claims 1-11 in which the zona pellucida of the blastocyst has been at least partially digested prior to step ii).

13. (Currently Amended) The A method of according to claim 12, wherein in which the zona pellucida of the blastocyst has been at least partially digested with a digestive agent selected from the group comprising acidic reacting substances, enzymes and mixtures thereof.

14. (Currently Amended) The A method of claim 1, wherein according to any of the claims 1-13 in which step ii) and/or step iv) is performed in an agent that improves the attachment of the blastocysts, and/or if relevant the inner cell mass cells to the feeder cells.

15. (Currently Amended) The A method of according to claim 14, wherein the agent is a hyaluronic acid.

16. (Currently Amended) The A method of claim 1, wherein according to any of the claims 1-15 in which the feeder cells are embryonic feeder cells.

17. (Currently Amended) The A method of claim 1, wherein according to any of the claims 1-16 in which the feeder cells employed in steps ii) and iv) are the same or different and the feeder cells originate from animal source.

18. (Currently Amended) The A method of according to claim 17, wherein the feeder cells are of mouse or human origin.

19. (Currently Amended) The A method of claim 1 according to any of the claims 1-18, wherein the feeder cells are mitotically inactivated.

20. (Currently Amended) The A method of claim 1 according to any of the claims 1-19, wherein the stem cell line

- i) exhibits proliferation capacity in an undifferentiated state for more than 21 months when grown on mitotically inactivated embryonic feeder cells; ~~and~~
- ii) exhibits normal euploid chromosomal karyotype; ~~and~~
- iii) maintains potential to develop into derivatives of all types of germ layers both *in vitro* and *in vivo*; ~~and~~
- iv) exhibits at least two of the group of following molecular markers consisting of OCT-4, alkaline phosphatase, ~~the carbohydrate epitopes~~ SSEA-3, SSEA-4, TRA 1-60, TRA 1-81, and the protein core of a keratin sulfate/chondroitin sulfate

pericellular matrix proteoglycan recognized by the monoclonal antibody GCTM-2;
and

v) does not exhibit molecular marker SSEA-1 or other differentiation markers; [[,]]
and

vi) retains its pluripotency and forms teratomas in vivo when injected into
immuno-compromised mice; [[,]] and

vii) is capable of differentiation differentiate.

21. (Currently Amended) ~~A Use of the human blastocyst-derived stem cell line obtained by the method of claim 1 according to any of the claims 1-20 for the preparation of differentiated cells.~~

22. (Currently Amended) ~~The A method according to any of claim 1 the claims 1-20, wherein the stem cell line has the ability of differentiating into an insulin producing cells.~~

23. (Currently Amended) ~~The A method of according to claim 22, wherein the insulin producing cells form are capable of forming islet-like structures.~~

24. (Currently Amended) ~~The A method of claim 22 according to claims 22 or 23, wherein the amount of insulin producing β -cells which is are derived from the pluripotent human BS cell line is higher than 25%, such as e.g. higher than 35%, or higher than 40%, or higher than 45%, or higher than 50%.~~

25. (Currently Amended) ~~The A method of claim 22 according to claims 22-24, wherein the insulin producing cell line produces at least about 300 ng insulin/mg total protein such as at least about 380 ng insulin/mg total protein or at least about 450 ng insulin/mg total protein.~~

26. (Currently Amended) ~~The A method according to any of claim 1 the claims 1-20 or 22-25, wherein the blastocyst-derived stem cells have the ability to differentiate into differentiated cells, which display the expression of pancreatic cell~~

type markers, including at least one of a group consisting of insulin, Glut-2, Pdx-1, glucokinase, glucagons, and somatostatin.

27. (Currently Amended) ~~The A method according to any of claim 1 the claims 1-20 or 22-26~~, wherein the blastocyst-derived stem cells have the ability to differentiate into insulin-producing cells that organize ~~characterized by their organization~~ into islet-like structures comprising an inner core of β -cells surrounded by an outer layer of neuron-type cells, which neuron-type cells display expression of at least one of the following neuronal cell type markers, including neuron-specific β -III tubulin (TUJ1), NeuN, DoubleCortin, tyrosine hydroxylase, and Map 2.

28. (Currently Amended) ~~The A method according to any of claim 1 the claims 1-20~~, wherein the blastocyst-derived stem cells are capable of being made into differentiated into cells, which express ~~display the expression of~~ at least one of ~~the following~~ neuronal cell type markers selected from the group consisting of , including neuron-specific β -III tubulin (TUJ1), NeuN, DoubleCortin, tyrosine hydroxylase, and Map 2.

29. (Currently Amended) ~~A Use of a preparation of differentiated cells derived from the blastocyst-derived stem cells obtained by the method according to any of claim 1 the claims 1-20 or 22-28 for the manufacture of a medicament for the preventing prevention or treating treatment of~~ pathologies or diseases caused by tissue degeneration.

30. (Currently Amended) ~~A Use of a preparation of differentiated cells derived from the blastocyst-derived stem cells obtained by the method according to any of claim 1 the claims 1-20 or 22-27 for the manufacture of a medicament for the preventing prevention or treating treatment of~~ pathologies or diseases in the pancreas.

31. (Currently Amended) The preparation of differentiated cells of Use according to claim 30, wherein in which the disease is diabetes.

32. (Currently Amended) The preparation of differentiated cells of Use according to claim 28 or 29, wherein in which the disease is type 1 diabetes.

33. (Currently Amended) A Use of a preparation of differentiated cells derived from the blastocyst-derived stem cell line obtained by the method according to any of claim 1 the claims 1-20 or 28 for the manufacture of a medicament for preventing the prevention or treating treatment of pathologies or diseases in the nervous system.

34. (Currently Amended) The preparation of differentiated cells of Use according to claim 33, in which the disease is selected from the group consisting of multiple sclerosis ~~schlerosis~~, spinal chord injury, an encephalopathy ~~encephalopathies~~, Parkinson's disease, Huntingdon's disease, stroke, a traumatic brain injury ~~injuries~~, a hypoxia induced brain injury ~~injuries~~, an ischemia induced brain injury ~~injuries~~, a hypoglycemic brain injury ~~injuries~~, a degenerative disorder ~~disorders~~ of the nervous system, a brain tumor, ~~tumors~~ and a neuropathy ~~neuropathies~~ in the peripheral nervous system.

35. (Currently Amended) A kit for performing the method according to any of claim 1 the claims 1-20, comprising human blastocysts with an intact zona pellucida or spontaneously hatched blastocysts, and at least two of the following components in separate compartments: [[;]] hyaluronic acid, pronase, BS-cell medium, and human or mouse embryonic feeder cells.

36. (Currently Amended) A method for producing an essentially pure preparation of insulin-producing differentiated stem cells, comprising: the steps of;
 i) expanding human blastocyst-derived stem cells by growing the blastocyst-derived stem cells ~~these~~ on an inactivated feeder cell layer in a suitable medium;
 ii) generating blastocyst-derived stem cell bodies by dissociating colonies formed in step i) into smaller aggregates or individual cells, followed by transferring said

aggregates or individual cells in to non-adherent containers wherein ~~where they said aggregate or individual cells~~ are incubated in a suitable medium;

iii) plating the blastocyst-derived stem cell bodies in containers in a suitable medium;

iv) selecting nestin-positive neural precursors in ITFSn medium;

v) expanding pancreatic endocrine progenitor cells in[[,]] N2-medium comprising B27 media complement and basic fibroblast growth factor; and

vi) changing the medium to a basic fibroblast growth factor-free N2 medium.

37. (Currently Amended) The A method of ~~according to~~ claim 36, wherein ~~in which~~ the human blastocyst-derived stem cells are obtained by ~~the method according to any of the claims 1-20;~~

i) using a fertilized oocyte of grade 1 or 2 to obtain a blastocyst of grade A or B;

ii) co-culturing the blastocyst with feeder cells to establish one or more colonies of inner cell mass cells;

iii) isolating the inner cell mass cells by mechanical dissection; and

iv) co-culturing the inner cell mass cells with feeder cells to obtain a blastocyst-derived stem cell line.

38. (Currently Amended) The A method of claim 36, wherein ~~according to claims 36-37~~ in which the medium used in step i) is human blastocyst-derived stem cell medium.

39. (Currently Amended) The A method of ~~according to~~ claim 36, wherein ~~38 in which~~ the medium used in step ii) is blastocyst-derived stem cell body medium.

40. (Currently Amended) The A method of claim 36, wherein ~~according to claims 36-39~~ in which the medium used in step iii) is blastocyst-derived stem cell body medium.

41. (Currently Amended) The A method of claim 36, wherein ~~according to claims 36-40~~ in which nicotinamide is added after step vi).

42. (Currently Amended) An essentially pure preparation of differentiated stem cells, wherein said stem the cells display an ~~the~~ expression of pancreatic cell type markers wherein said marker is ~~, including~~ at least one or more of insulin, Glut-2, Pdx-1, glucokinase, glucagons, or ~~and~~ somatostatin.

43. (Currently Amended) The preparation of ~~according to~~ claim 42, which is capable of producing at least about 320 ng insulin/mg total protein ~~such as at least about 380 ng insulin/mg total protein or at least about 420 ng insulin/mg total protein.~~

44. (Currently Amended) The preparation of claim 42, wherein the ~~according to claims 42 or 43, in which preparation~~ comprises at least 25% the ~~proportion of insulin producing cells is at least 25%, such as e.g. at least 35%, or at least 45%, or at least 50%.~~

45. (Currently Amended) The preparation of claim 42, wherein said stem ~~cells are organized according to claims 42-44, characterized by its organization into~~ islet-like structures comprising an inner core of β -cells surrounded by an outer layer of neuron-type cells, wherein the ~~which~~ neuron-type cells express ~~display expression~~ of at least one of the ~~following~~ neuronal cell type markers selected from the group consisting of: ~~, including~~ neuron-specific β -III tubulin (TUJ1), NeuN, DoubleCortin, tyrosine hydroxylase, and Map 2.

46. (Currently Amended) The preparation of claim 42 ~~according to claims 42-45, obtained by the method according to claims 36-41:~~

- i) expanding human blastocyst-derived stem cells by growing the blastocyst-derived stem cells on an inactivated feeder cell layer in a suitable medium;
- ii) generating blastocyst-derived stem cell bodies by dissociating colonies formed in step i) into smaller aggregates or individual cells, followed by transferring said aggregates or individual cells in to non-adherent containers wherein said aggregate or individual cells are incubated in a suitable medium; and

- iii) plating the blastocyst-derived stem cell bodies in containers in a suitable medium;
- iv) selecting nestin-positive neural precursors in ITFSn medium;
- v) expanding pancreatic endocrine progenitor cells in N2-medium comprising B27 media complement and basic fibroblast growth factor; and
- vi) changing the medium to a basic fibroblast growth factor-free N2 medium.

47. (Currently Amended) An essentially pure preparation of differentiated stem cells, wherein the stem cells express ~~display the expression of~~ at least one of the following neuronal cell type markers selected from the group consisting of ; including neuron-specific β -III tubulin (TUJ1), NeuN, DoubleCortin, tyrosine hydroxylase, or and Map 2.

48. (Currently Amended) The preparation of ~~according to~~ claim 47~~[[,]]~~ obtained by ~~the method according to claims 36-41;~~
- i) expanding human blastocyst-derived stem cells by growing the blastocyst-derived stem cells on an inactivated feeder cell layer in a suitable medium;
 - ii) generating blastocyst-derived stem cell bodies by dissociating colonies formed in step i) into smaller aggregates or individual cells, followed by transferring said aggregates or individual cells in to non-adherent containers wherein said aggregate or individual cells are incubated in a suitable medium; and
 - iii) plating the blastocyst-derived stem cell bodies in containers in a suitable medium;
 - iv) selecting nestin-positive neural precursors in ITFSn medium;
 - v) expanding pancreatic endocrine progenitor cells in N2-medium comprising B27 media complement and basic fibroblast growth factor; and
 - vi) changing the medium to a basic fibroblast growth factor-free N2 medium.

49. (Currently Amended) An essentially pure preparation of stem cells obtained ~~obtainable by the method according to claims 36-41;~~
- i) expanding human blastocyst-derived stem cells by growing the blastocyst-derived stem cells on an inactivated feeder cell layer in a suitable medium;

- ii) generating blastocyst-derived stem cell bodies by dissociating colonies formed in step i) into smaller aggregates or individual cells, followed by transferring said aggregates or individual cells in to non-adherent containers wherein said aggregate or individual cells are incubated in a suitable medium; and
- iii) plating the blastocyst-derived stem cell bodies in containers in a suitable medium;
- iv) selecting nestin-positive neural precursors in ITFSn medium;
- v) expanding pancreatic endocrine progenitor cells in N2-medium comprising B27 media complement and basic fibroblast growth factor; and
- vi) changing the medium to a basic fibroblast growth factor-free N2 medium.

50. (Currently Amended) An essentially pure Use of a preparation of differentiated stem cells of claim 42 according to claims 42-46 for the manufacture of a medicament for the preventing prevention or treating treatment of pathologies or diseases in the pancreas.

51. (Currently Amended) The preparation of Use according to claim 50, wherein in which the disease is diabetes.

52. (Currently Amended) The preparation of Use according to claim 50, wherein or 51, in which the disease is type 1 diabetes.

53. (Currently Amended) The preparation of claim 47 Use of a preparation according to claims 47-48 for the manufacture of a medicament for treating the treatment of pathologies or diseases in the nervous system.

54. (Currently Amended) The preparation of Use according to claim 53, wherein in which the disease is selected from the group consisting of multiple sclerosis sehlerosis, spinal chord injury, an encephalopathy encephalopathies, Parkinson's disease, Huntingdon's disease, stroke, a traumatic brain injury injuries, a hypoxia induced brain injury injuries, an ischemia induced brain injury injuries, a hypoglycemic brain injury injuries, a degenerative disorder disorders of the nervous

system, a brain tumor, ~~tumors~~ and a neuropathy ~~neuropathies~~ in the peripheral nervous system.

55. (Currently Amended) A kit ~~Kit~~ for performing the method of claim 36 ~~according to claims 36-41~~, comprising at least two of the following components in separate compartments: [[;]] mitomycin C, hBS medium, BS cell body medium, ITSFn-medium, N2-medium, B27-media supplement, nicotinamide, and bFGF.

56. (Currently Amended) The kit ~~Kit according to~~ of claim 55, further comprising an essentially pure human blastocyst-derived ~~derived~~ stem cell line obtained by ~~the method according to any of the claims 1-20~~:

- i) using a fertilized oocyte of grade 1 or 2 to obtain a blastocyst of grade A or B;
- ii) co-culturing the blastocyst with feeder cells to establish one or more colonies of inner cell mass cells;
- iii) isolating the inner cell mass cells by mechanical dissection; and
- iv) co-culturing the inner cell mass cells with feeder cells to obtain a blastocyst-derived stem cell line.

57. (New) The method of claim 1 further comprising propagating the blastocyst-derived stem cell line.

58. (New) The method of claim 2 further comprising propagating the blastocyst-derived stem cell line.

59. (New) The method of claim 3 further comprising propagating the blastocyst-derived stem cell line.

60. (New) The method of claim 9, wherein the step of culturing uses feeder cells at a density less than about 55,000 cells per cm².

61. (New) The method of claim 9, wherein the step of culturing uses feeder cells at a density less than about 50,000 cells per cm².